Supporting Information

Synthesis of triazine dendrimers based on a divergent strategy using a trimethylene-dipiperidine linker to improve dendrimer solubility and increase reactivity towards monomer units

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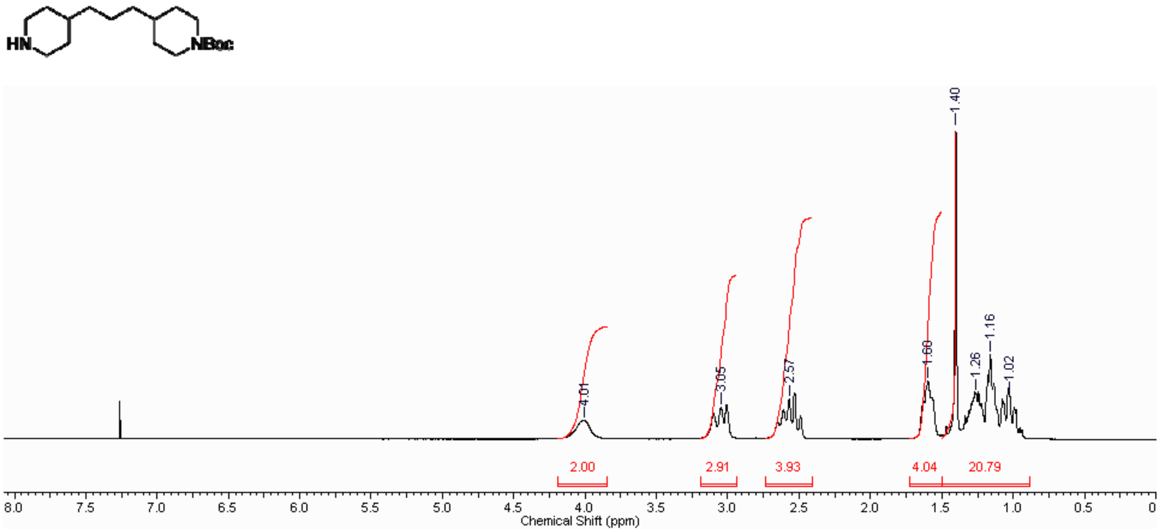


Figure S1. ^{1}H NMR spectrum of **S1** (300 MHz, $CDCl_3$).

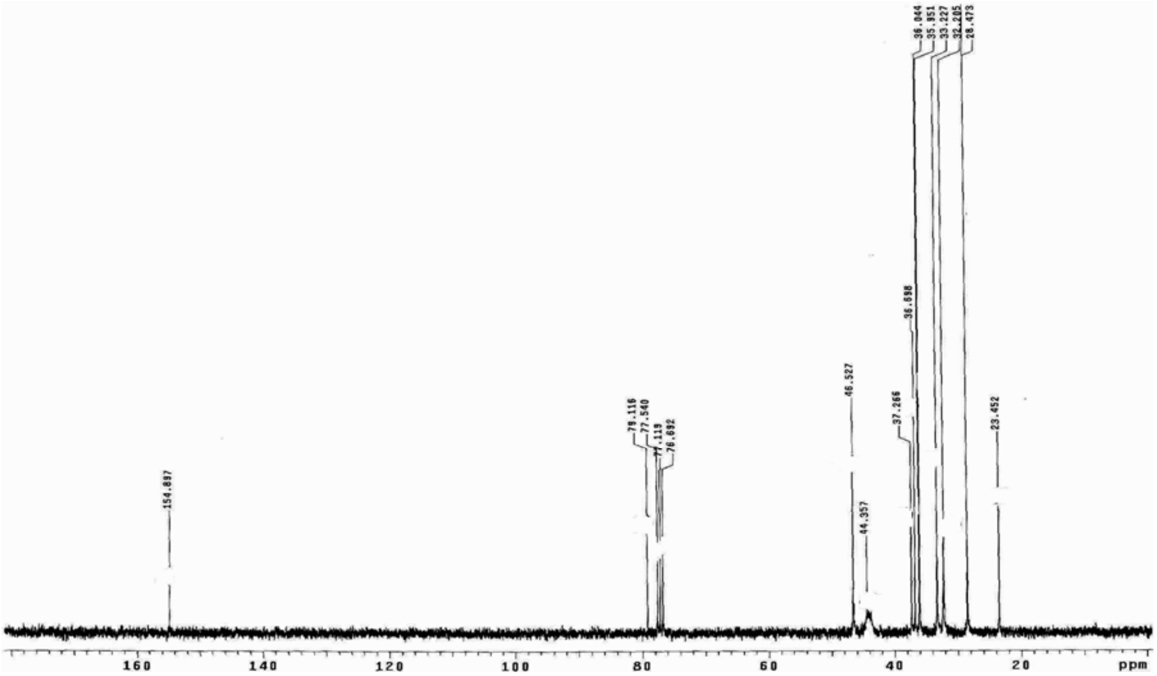


Figure S2. ^{13}C NMR spectrum of **S1** (75 MHz, $CDCl_3$).

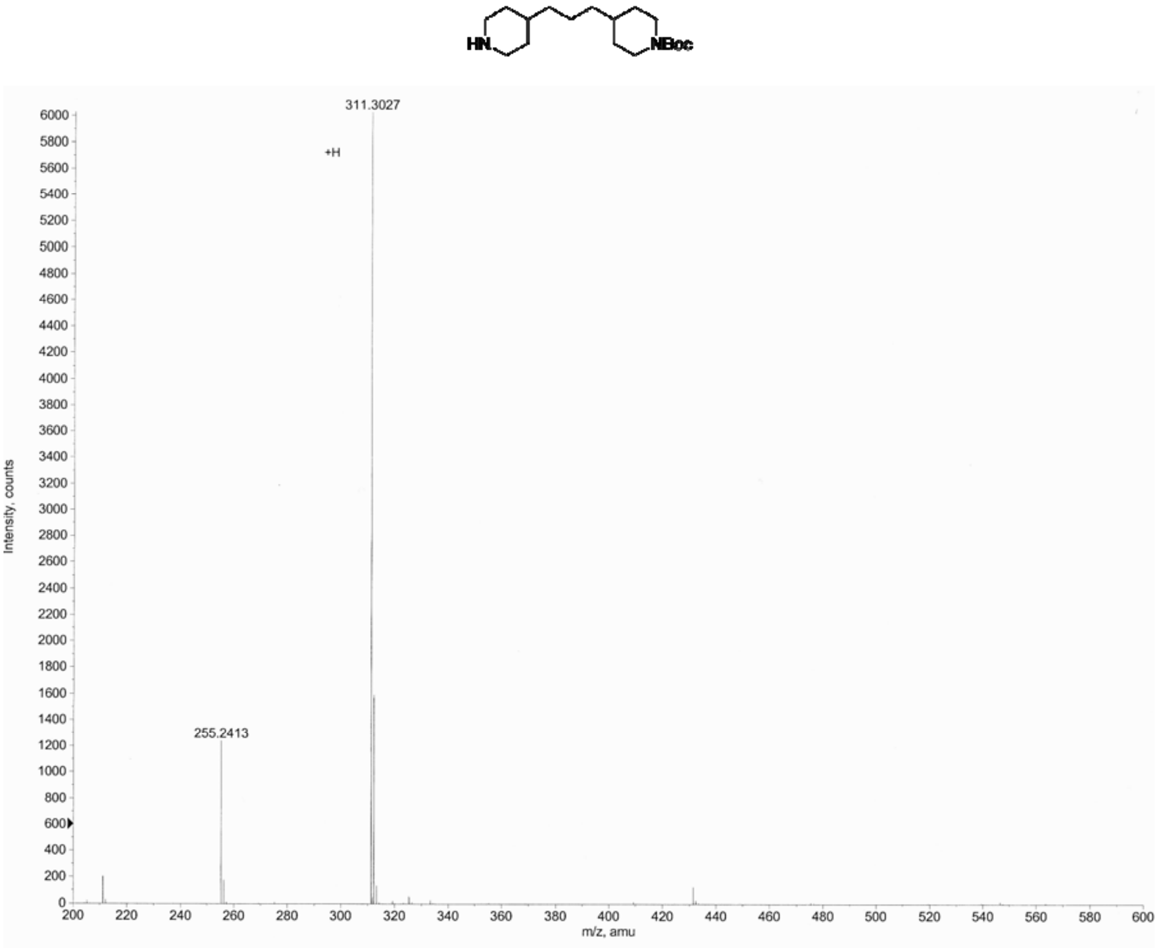
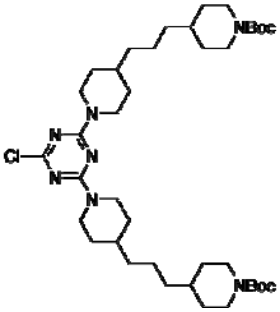


Figure S3. ESI-TOF mass spectrum of **S1**.



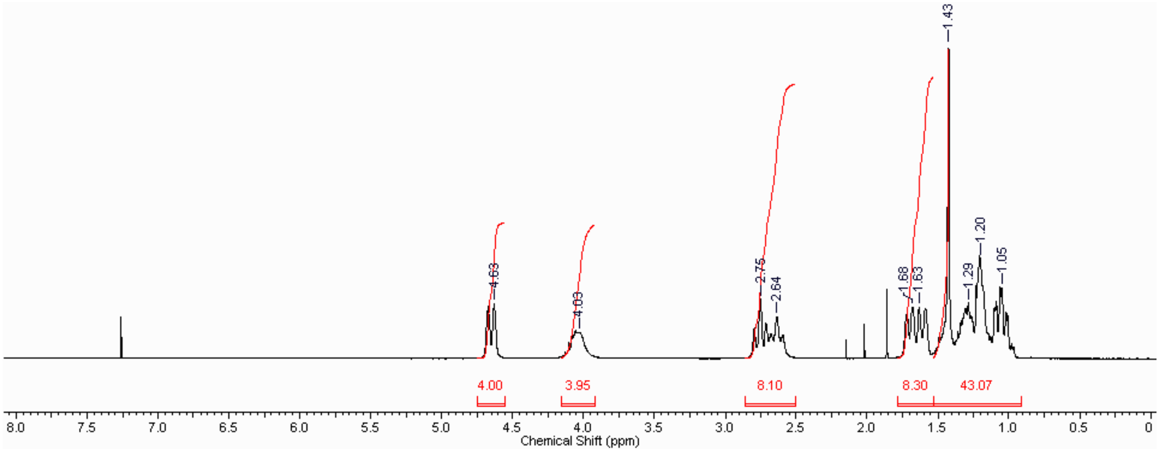


Figure S4. ^{1}H NMR spectrum of monochlorotriazine **1** (300 MHz, $CDCl_3$).

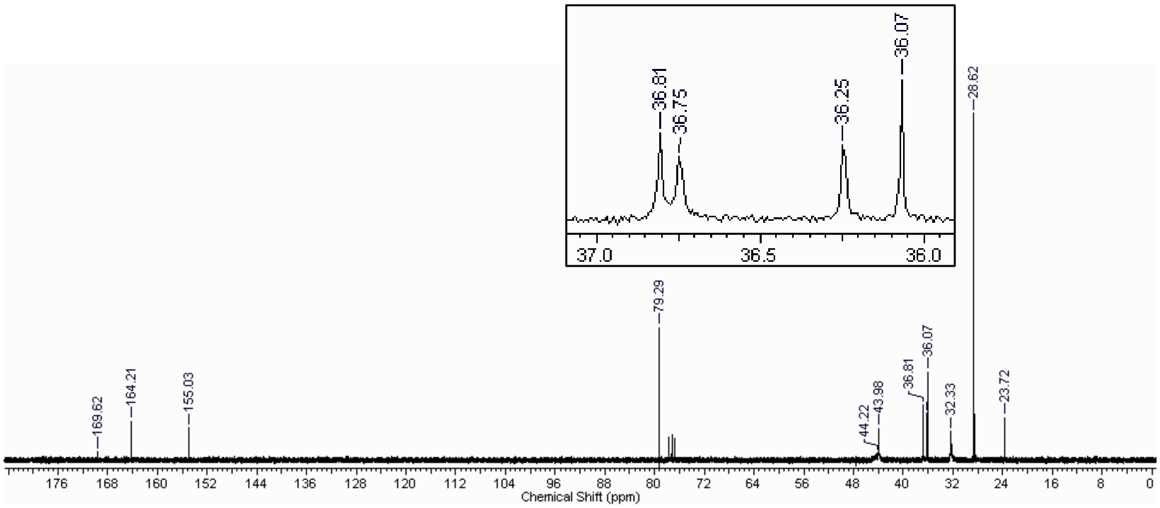
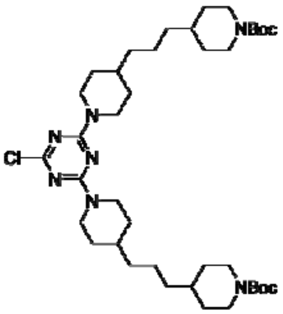


Figure S5. ^{13}C NMR spectrum of monochlorotriazine **1** (75 MHz, $CDCl_3$).



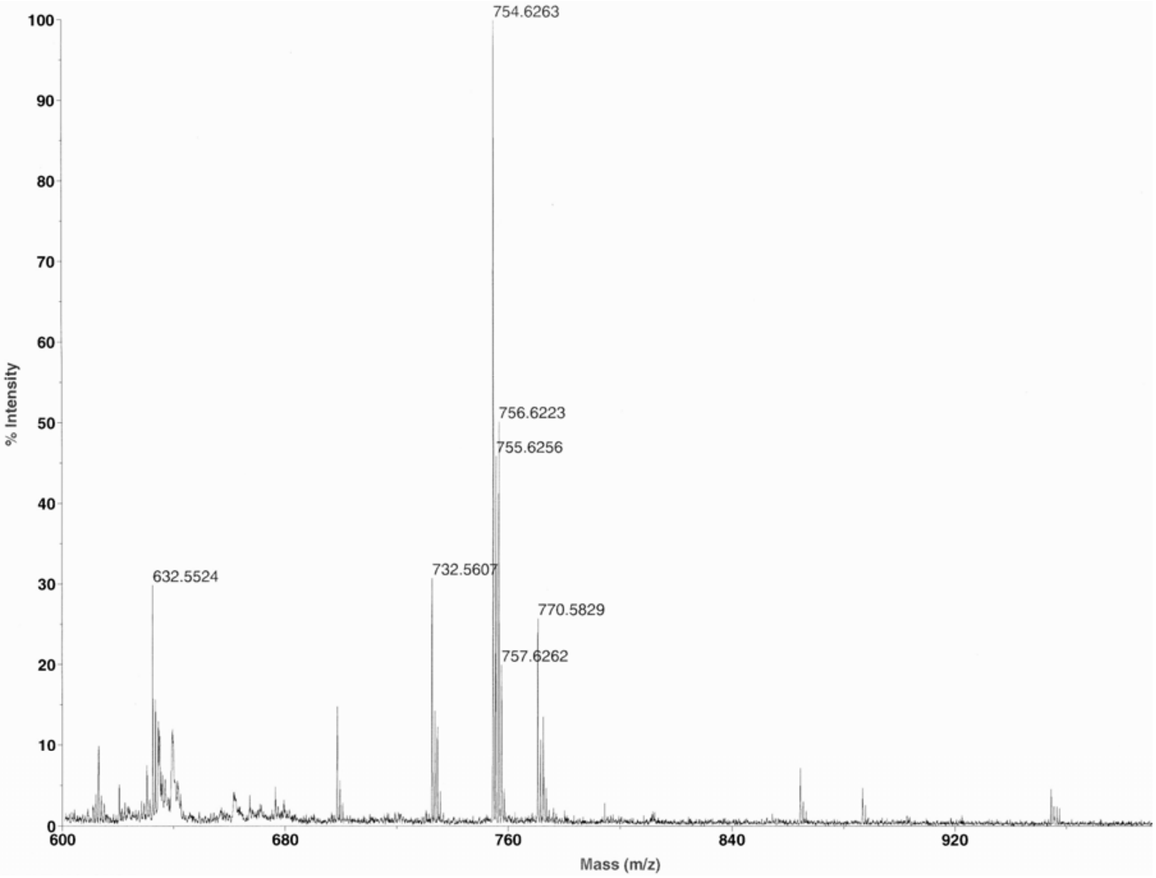
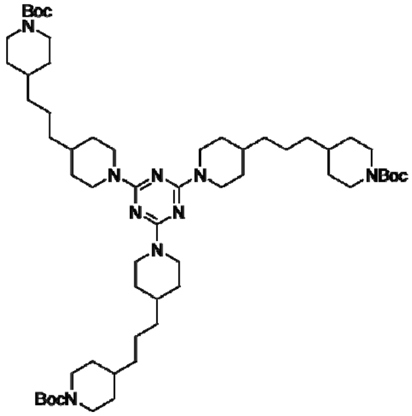


Figure S6. MALDI mass spectrum of monochlorotriazine **1**.



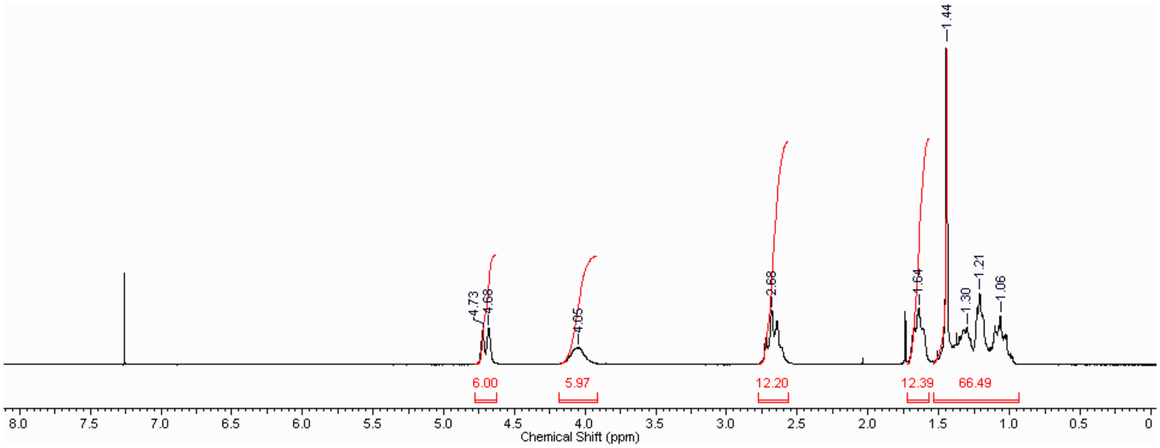


Figure S7. ^{1}H NMR spectrum of **3** (300 MHz, $CDCl_3$).

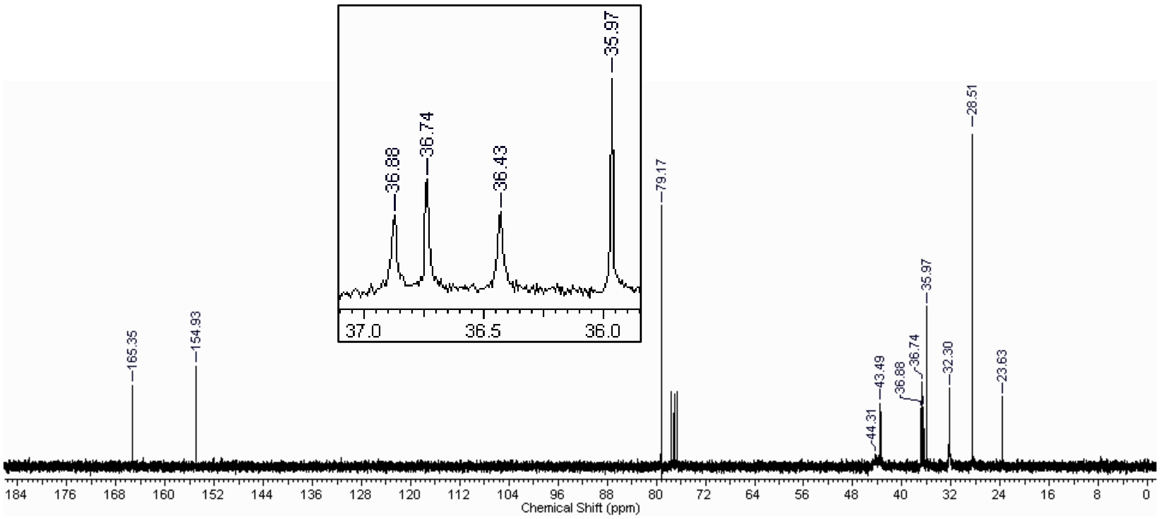
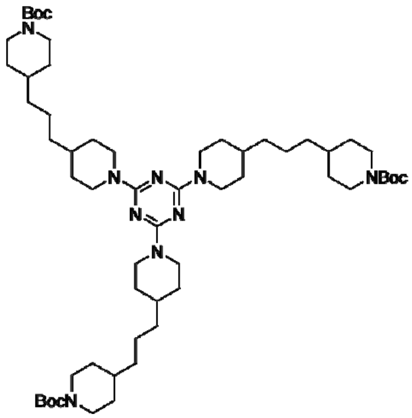


Figure S8. ^{13}C NMR spectrum of **3** (75 MHz, $CDCl_3$).



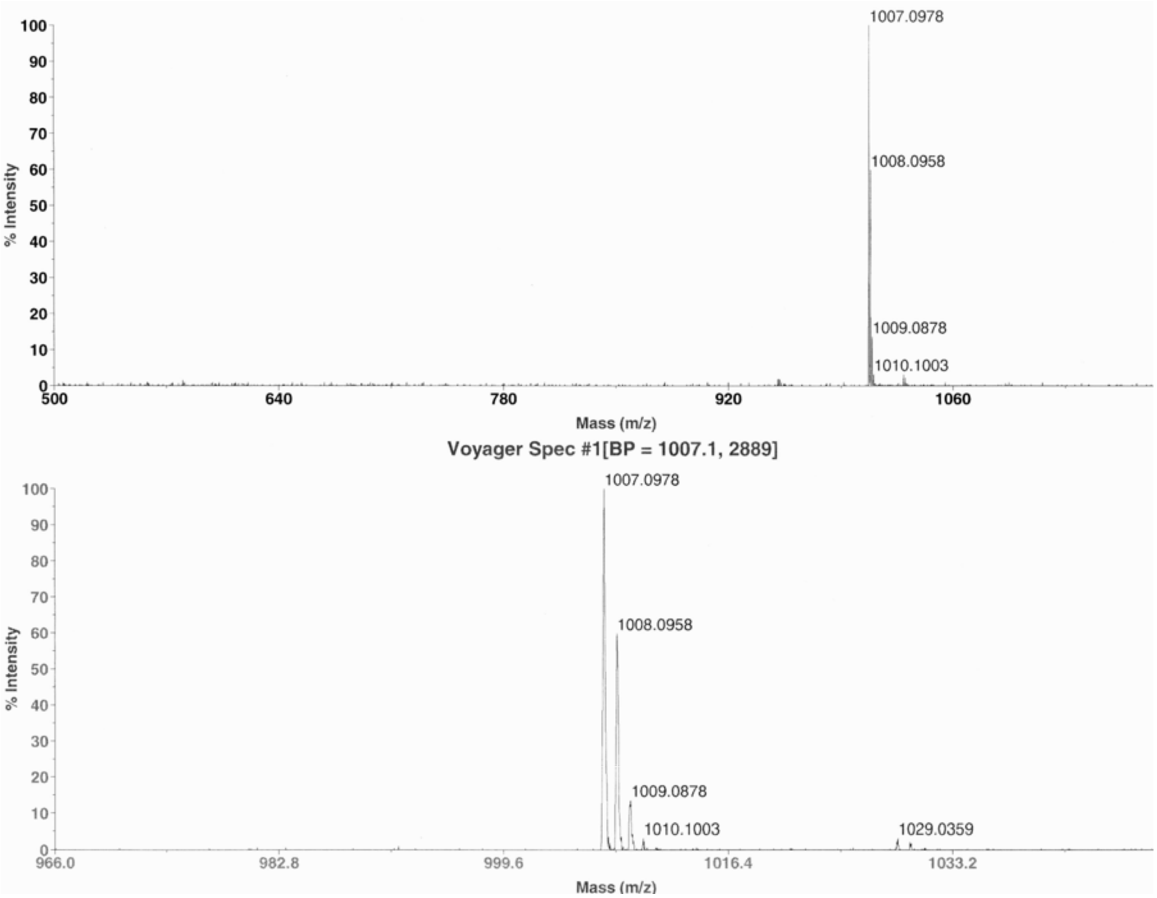
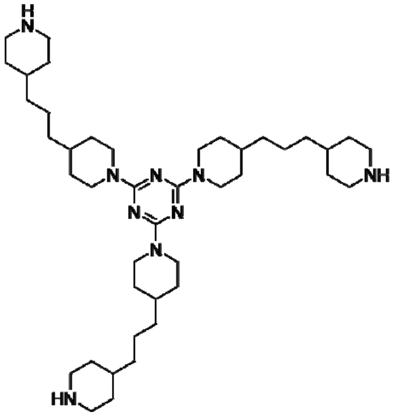


Figure S9. MALDI mass spectrum of **3**.



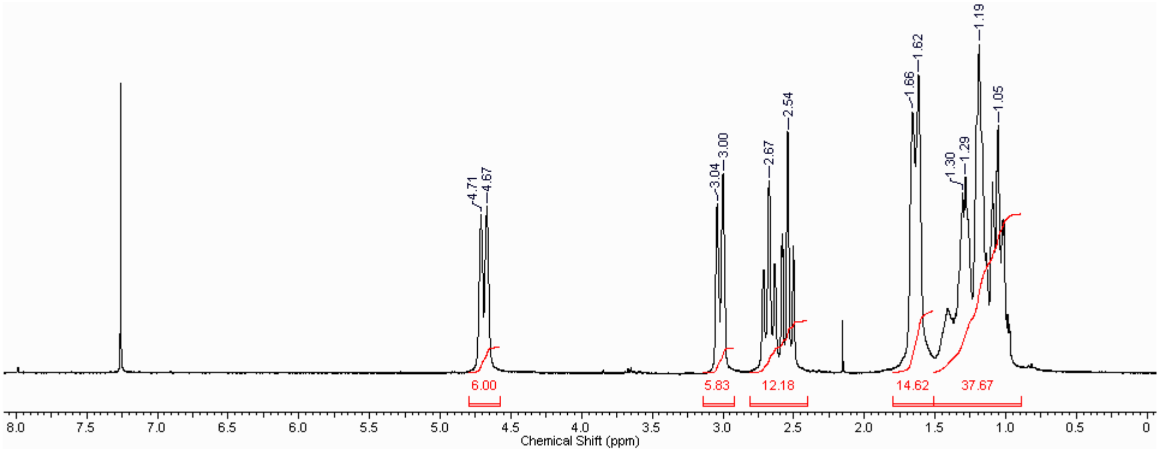


Figure S10. ^{1}H NMR spectrum of **4** (300 MHz, $CDCl_3$).

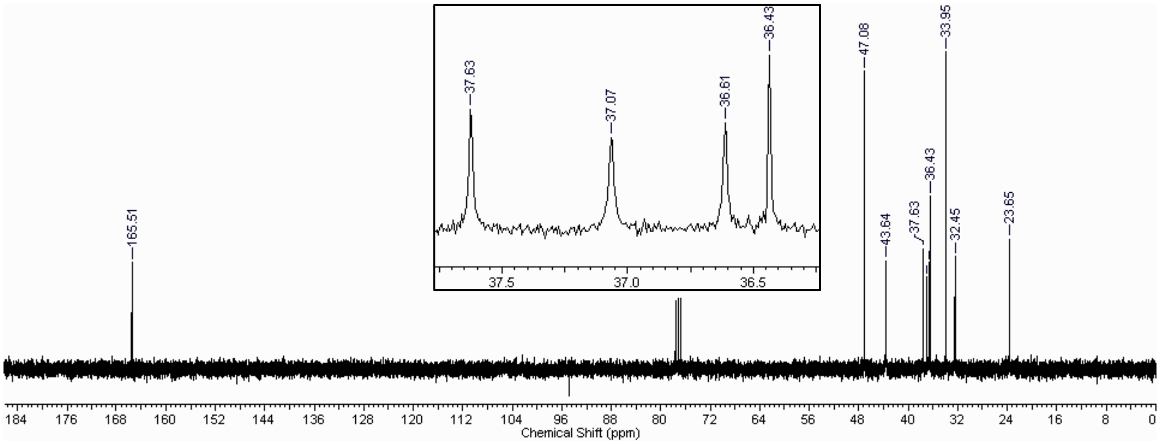
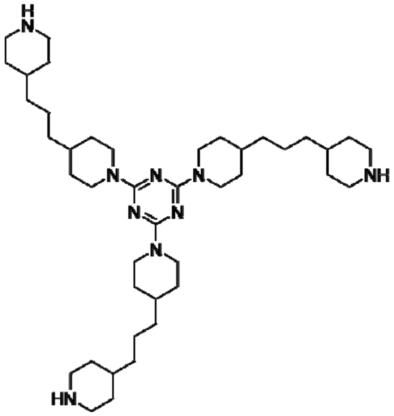


Figure S11. ^{13}C NMR spectrum of **4** (75 MHz, $CDCl_3$).



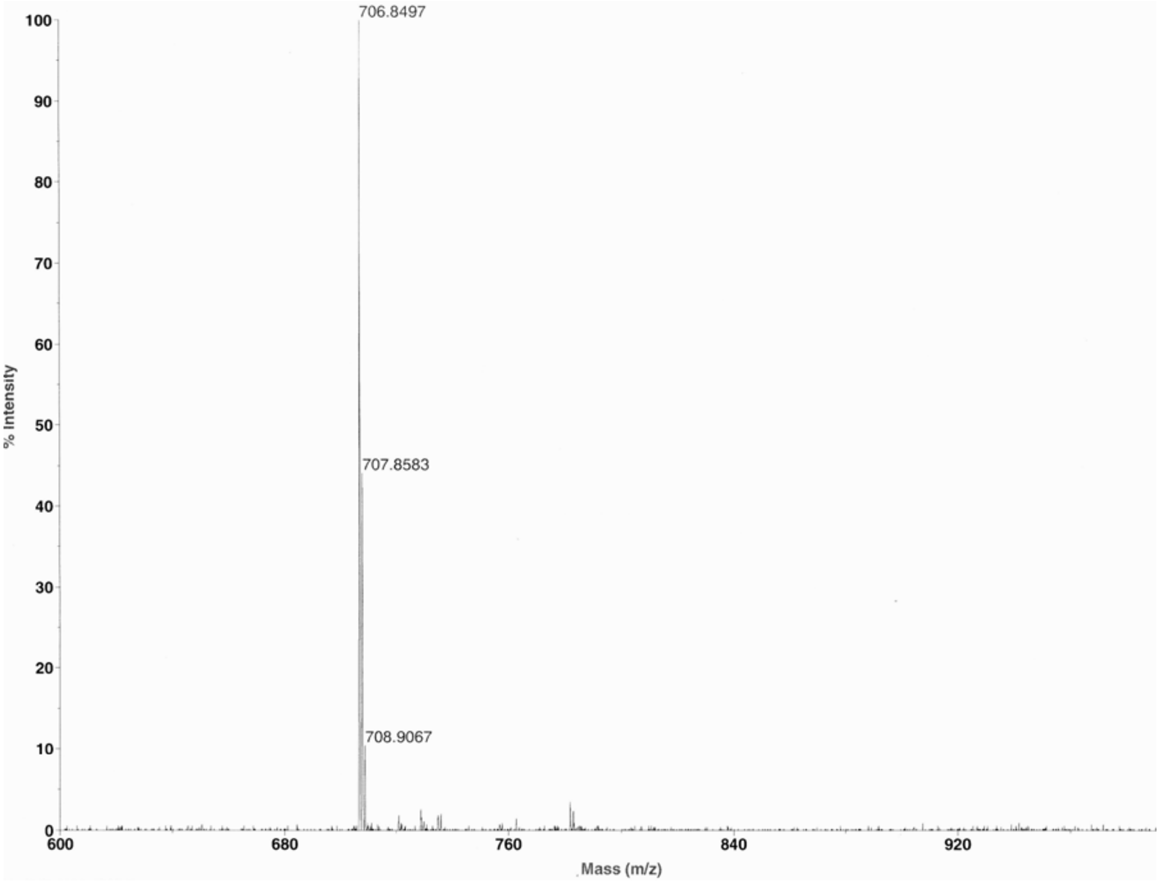
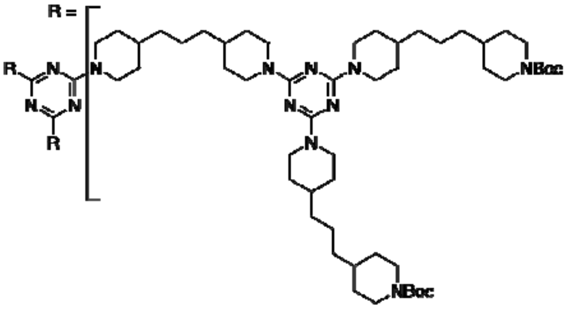


Figure S12. MALDI mass spectrum of **4**.



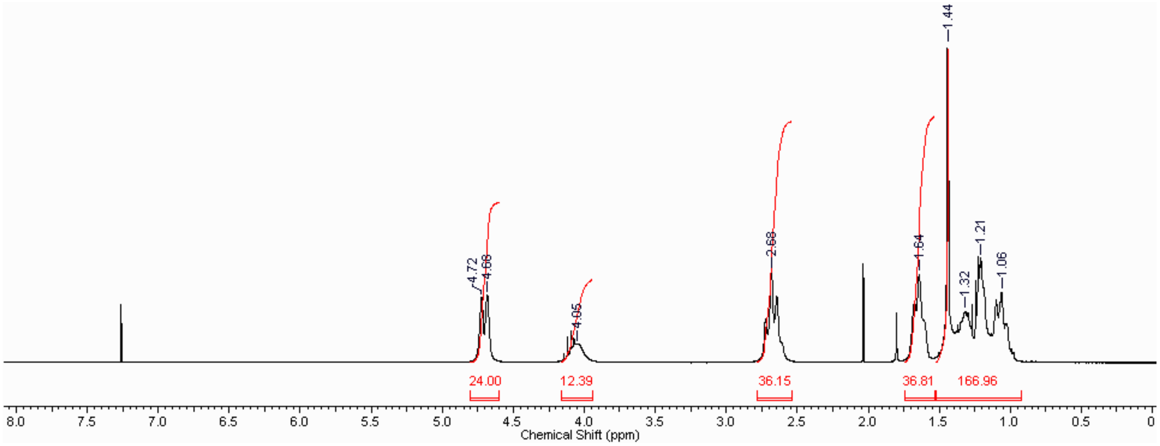


Figure S13. ^{1}H NMR spectrum of dendrimer **5** (300 MHz, $CDCl_3$).

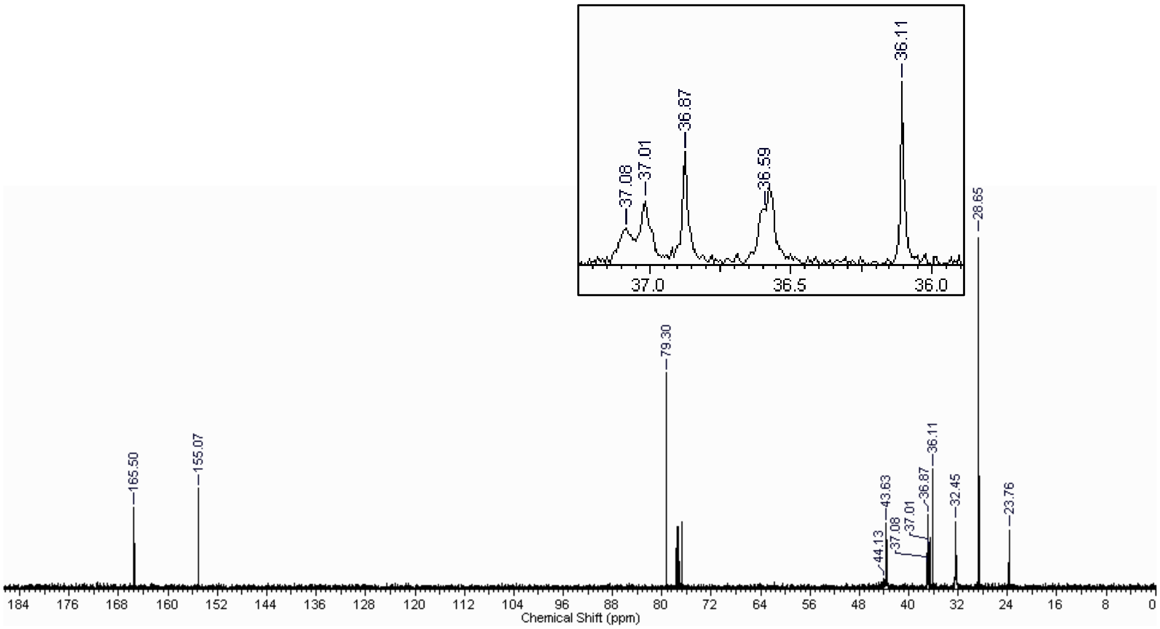


Figure S14. ^{13}C NMR spectrum of dendrimer **5** (75 MHz, $CDCl_3$).

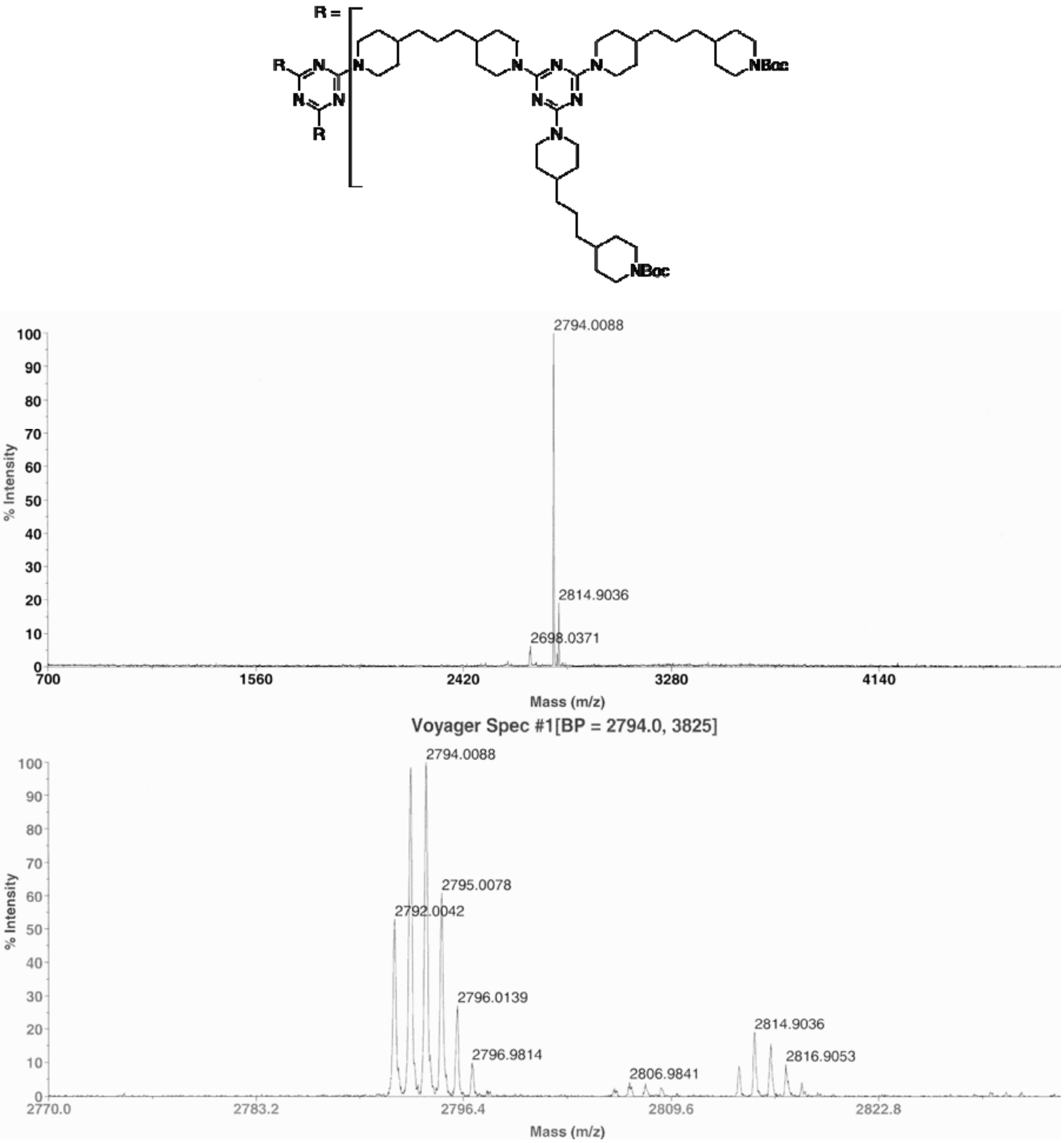
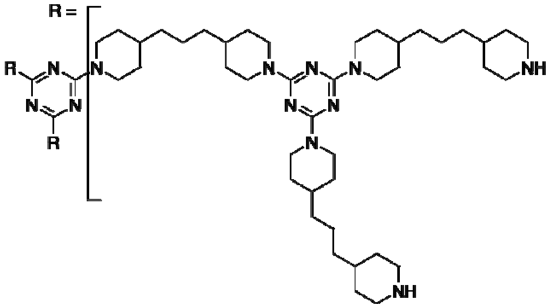


Figure S15. MALDI mass spectrum of dendrimer **5**.



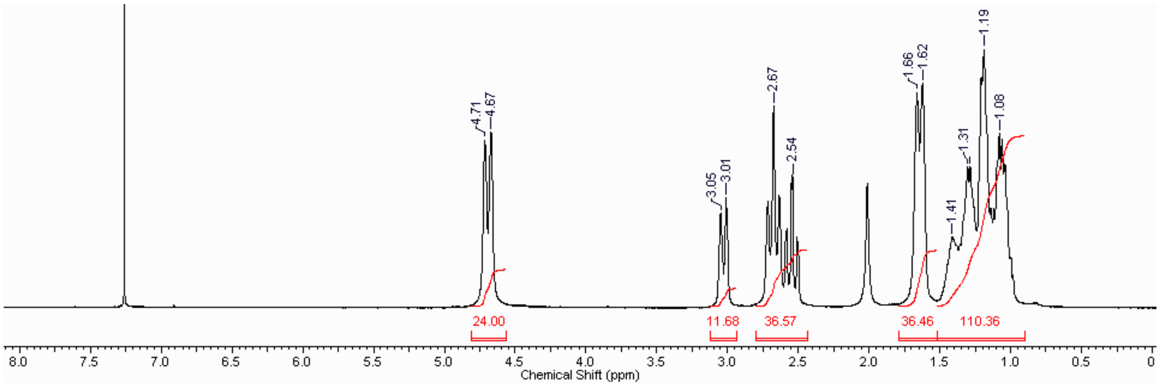


Figure S16. ^{1}H NMR spectrum of dendrimer **6** (300 MHz, $CDCl_3$).

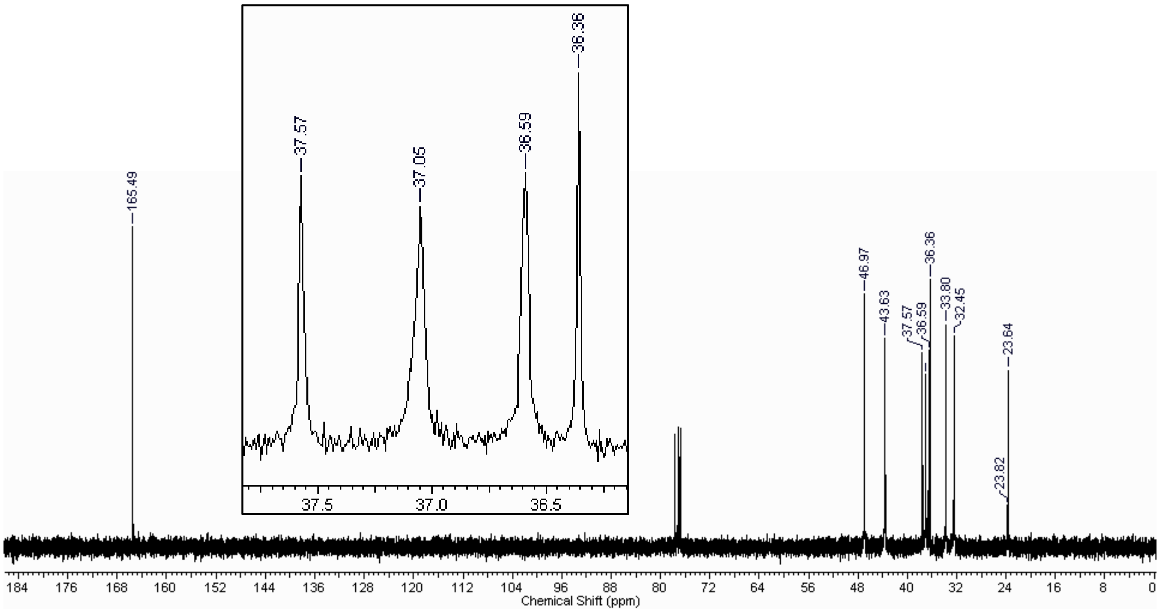


Figure S17. ^{13}C NMR spectrum of dendrimer **6** (75 MHz, $CDCl_3$).

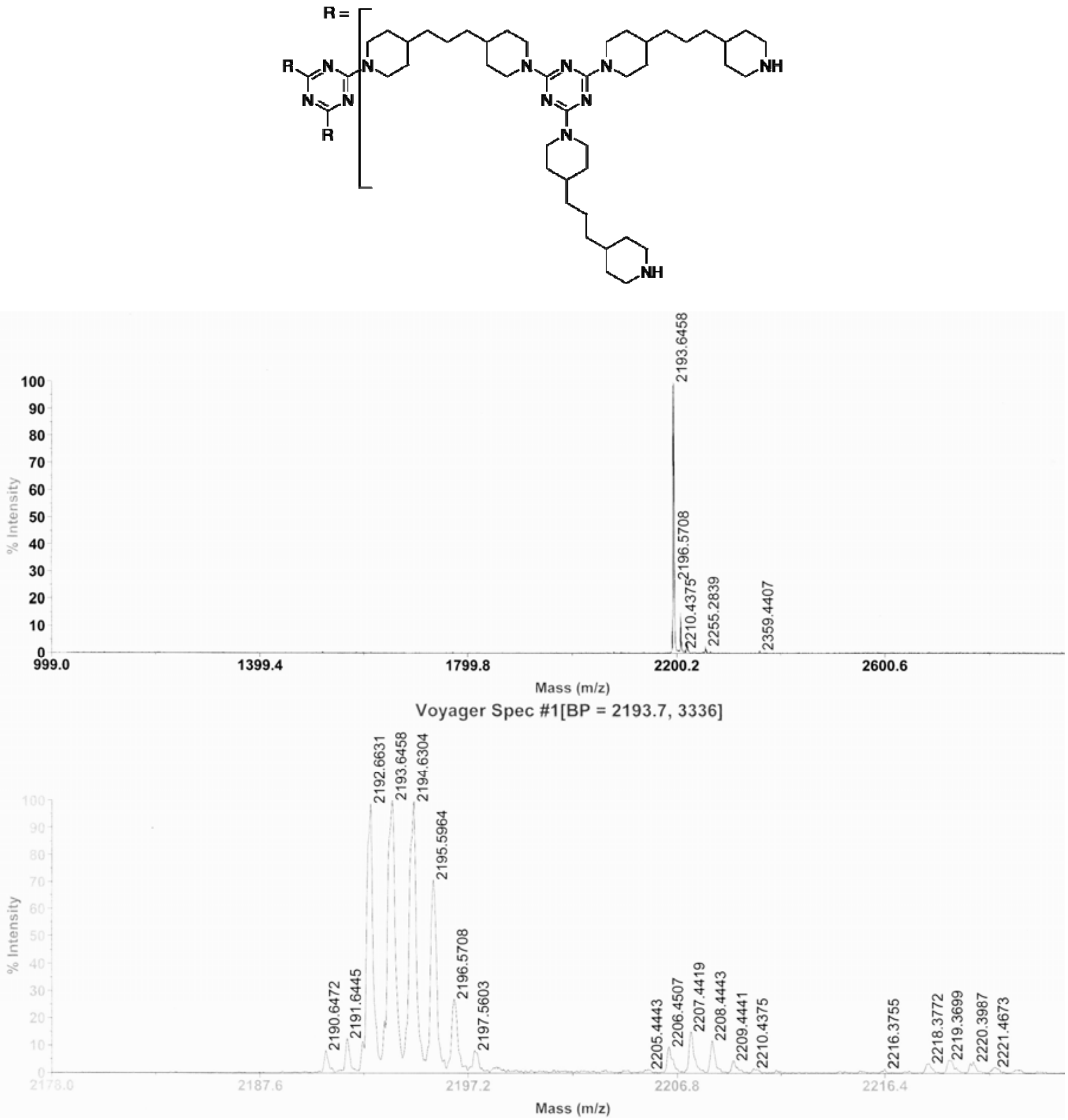
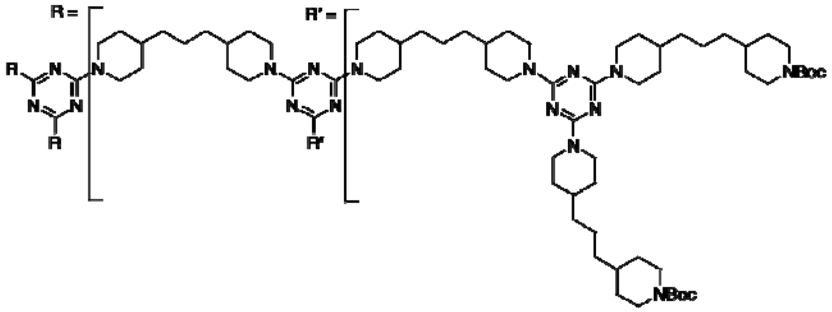


Figure S18. MALDI mass spectrum of dendrimer **6**.



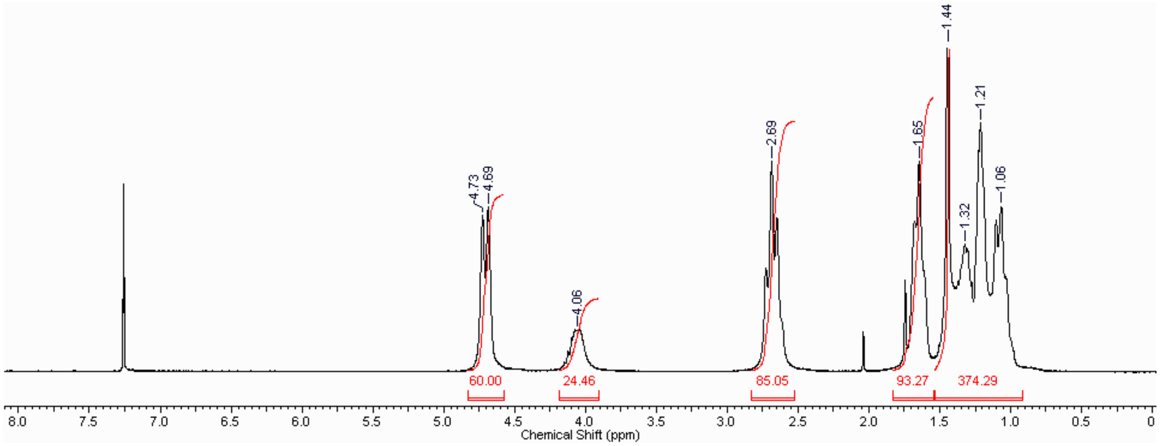


Figure S19. ^{1}H NMR spectrum of dendrimer **7** (300 MHz, $CDCl_3$).

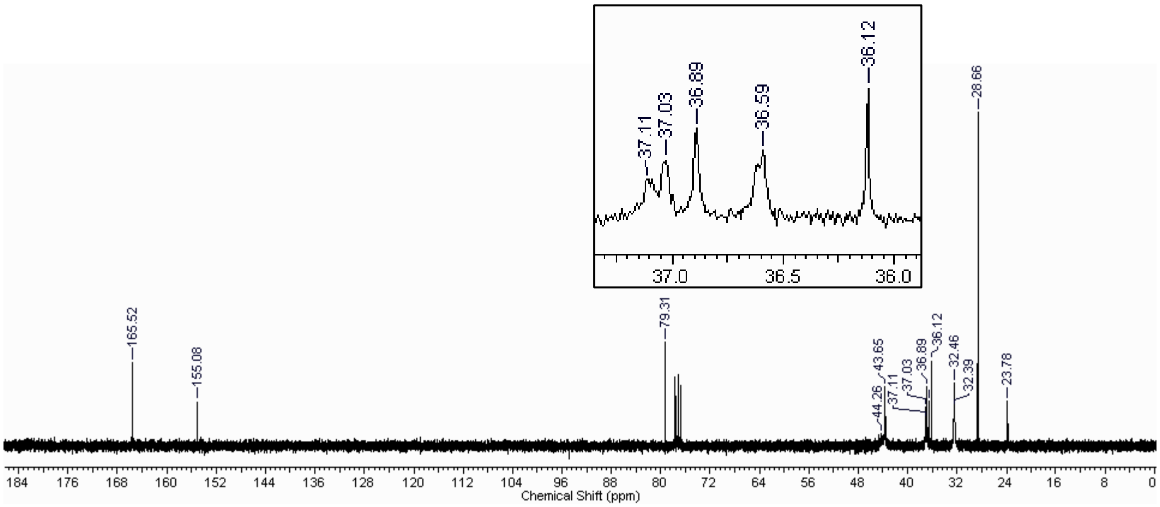


Figure S20. ^{13}C NMR spectrum of dendrimer **7** (75 MHz, $CDCl_3$).

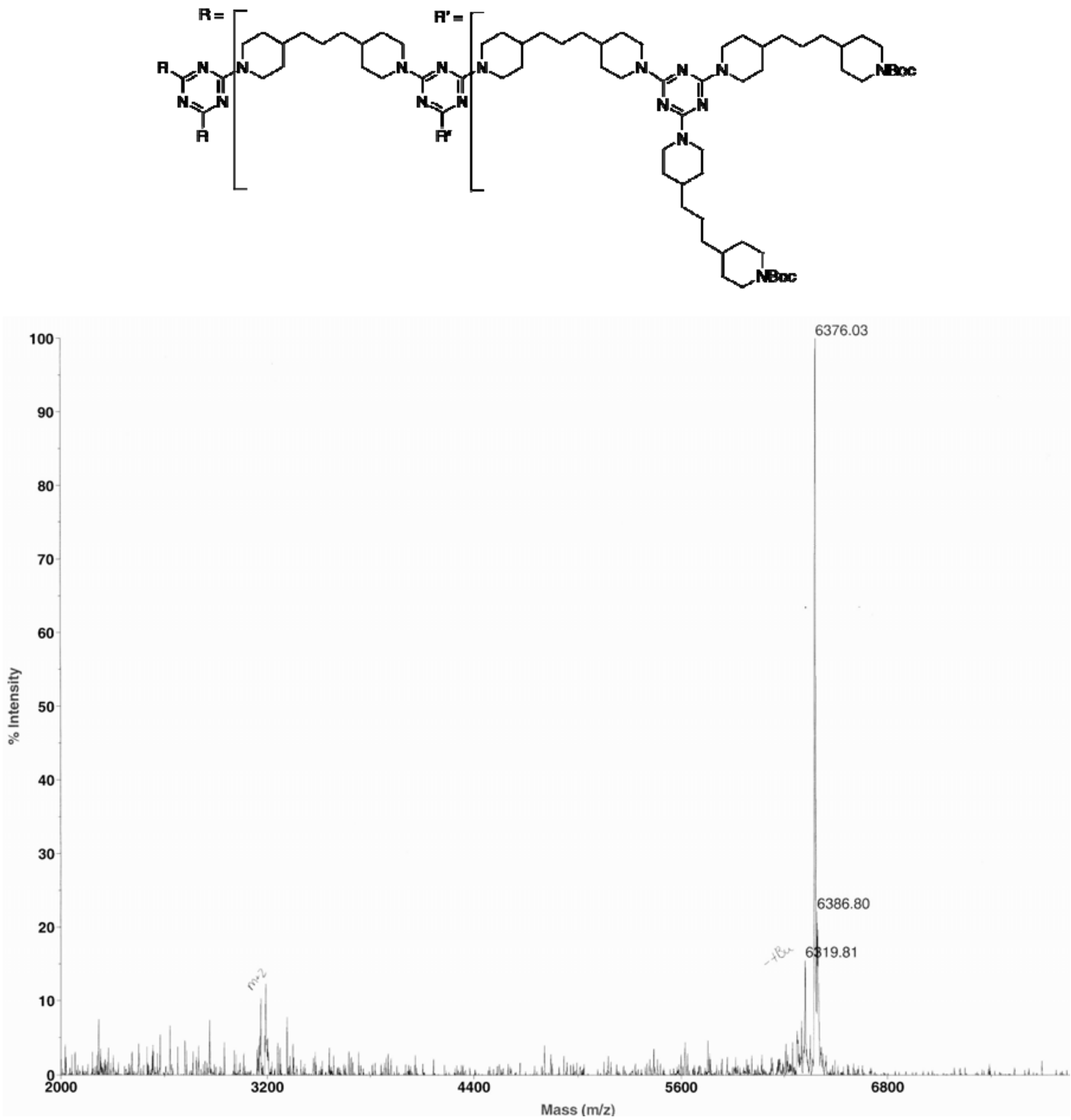
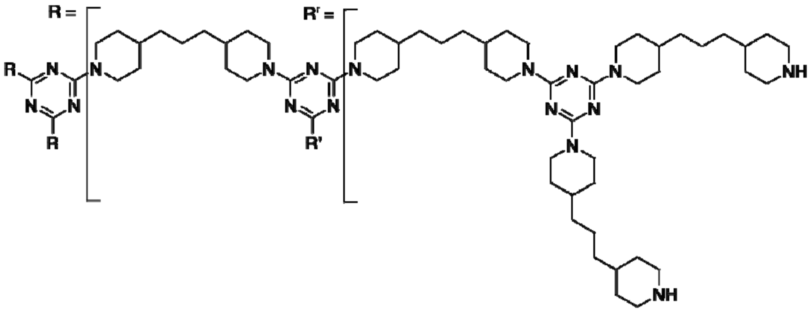


Figure S21. MALDI mass spectrum of dendrimer **7**.



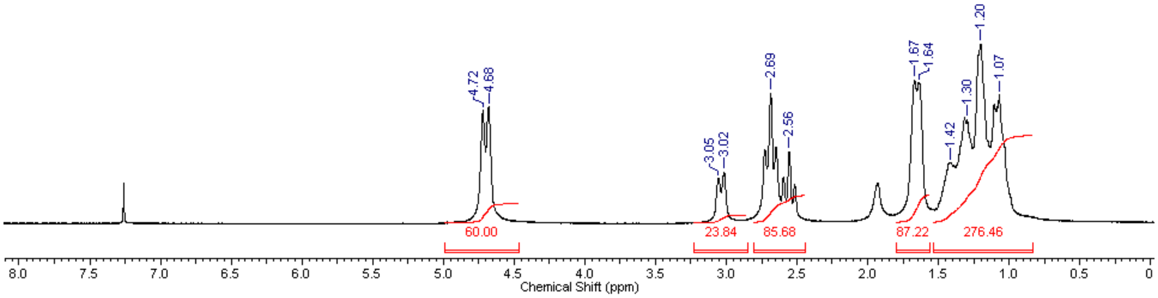


Figure S22. ^{1}H NMR spectrum of dendrimer **8** (300 MHz, $CDCl_3$).

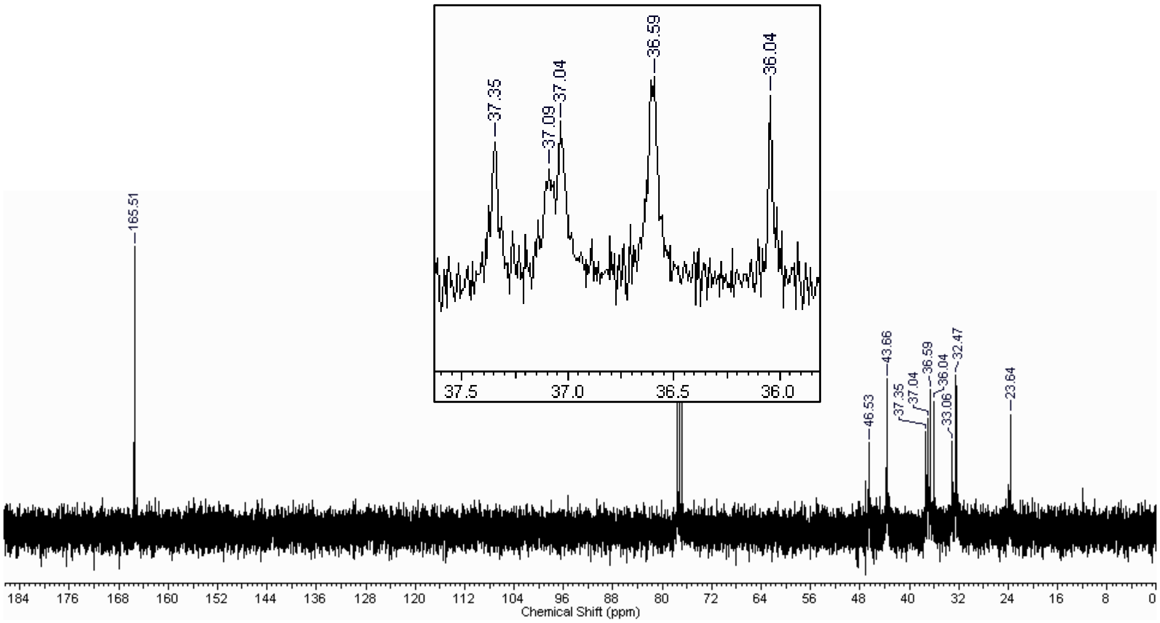


Figure S23. ^{13}C NMR spectrum of dendrimer **8** (75 MHz, $CDCl_3$).

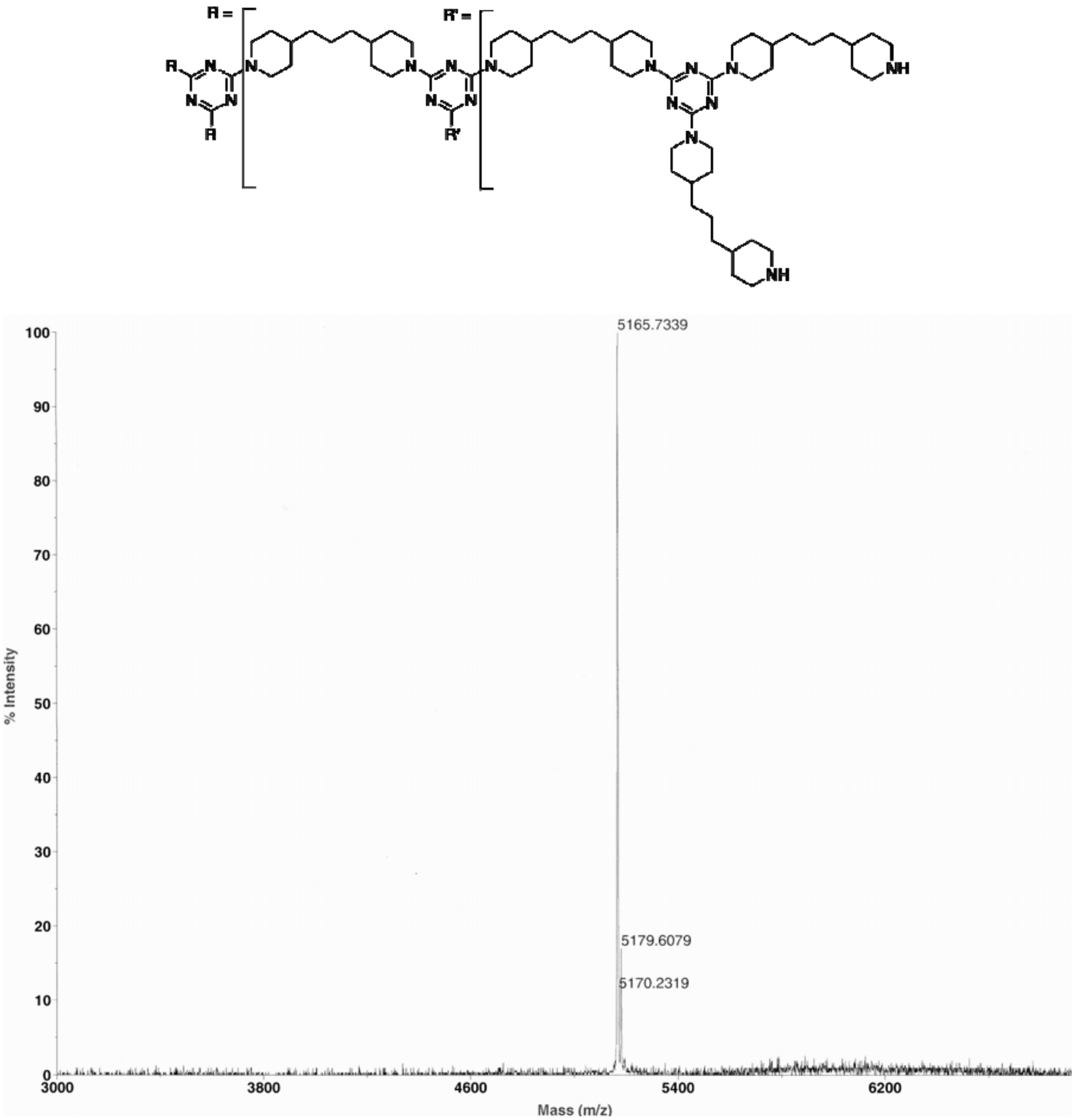
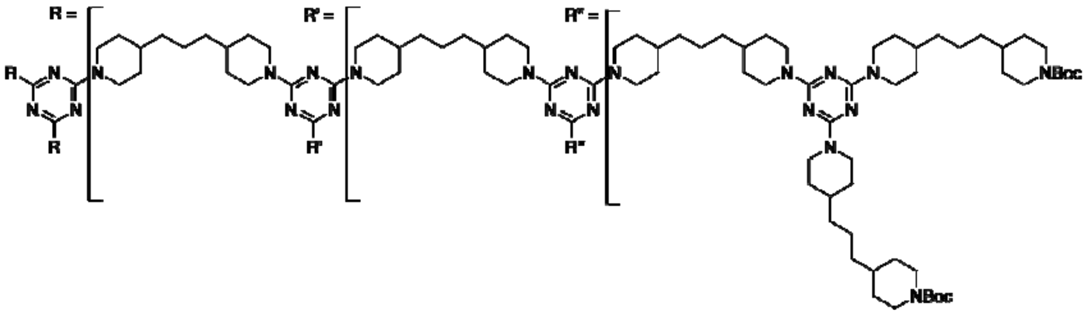


Figure S24. MALDI mass spectrum of dendrimer **8**.



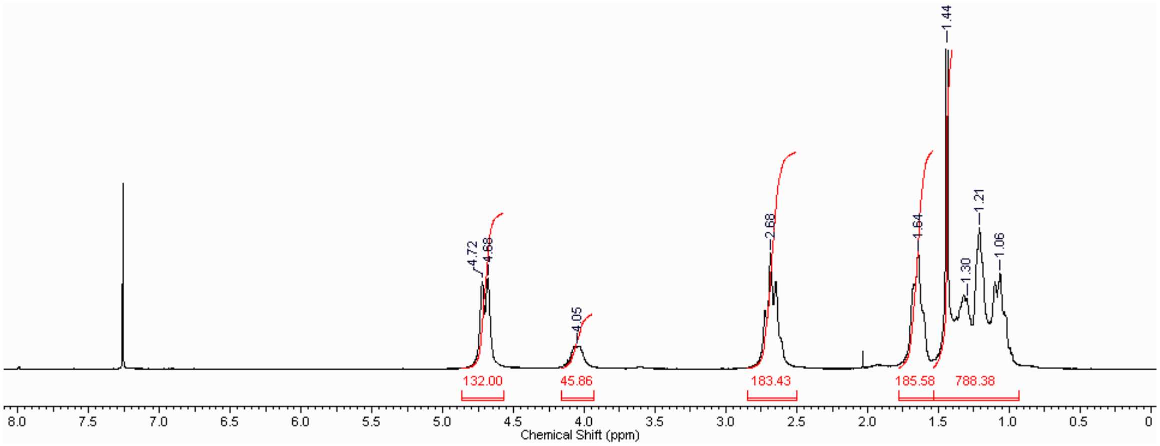


Figure S25. ^{1}H NMR spectrum of dendrimer **9** (300 MHz, $CDCl_3$).

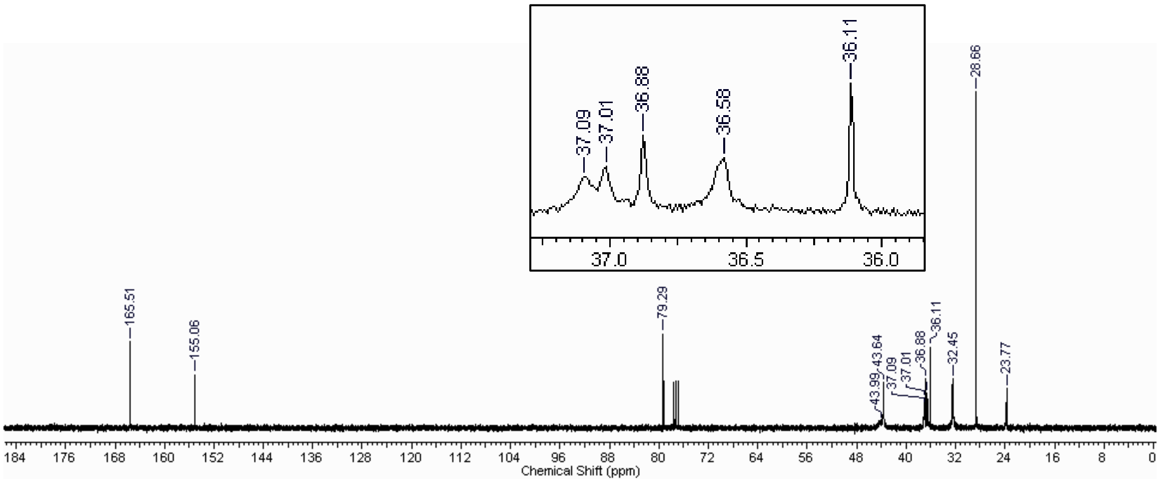


Figure S26. ^{13}C NMR spectrum of dendrimer **9** (75 MHz, $CDCl_3$).

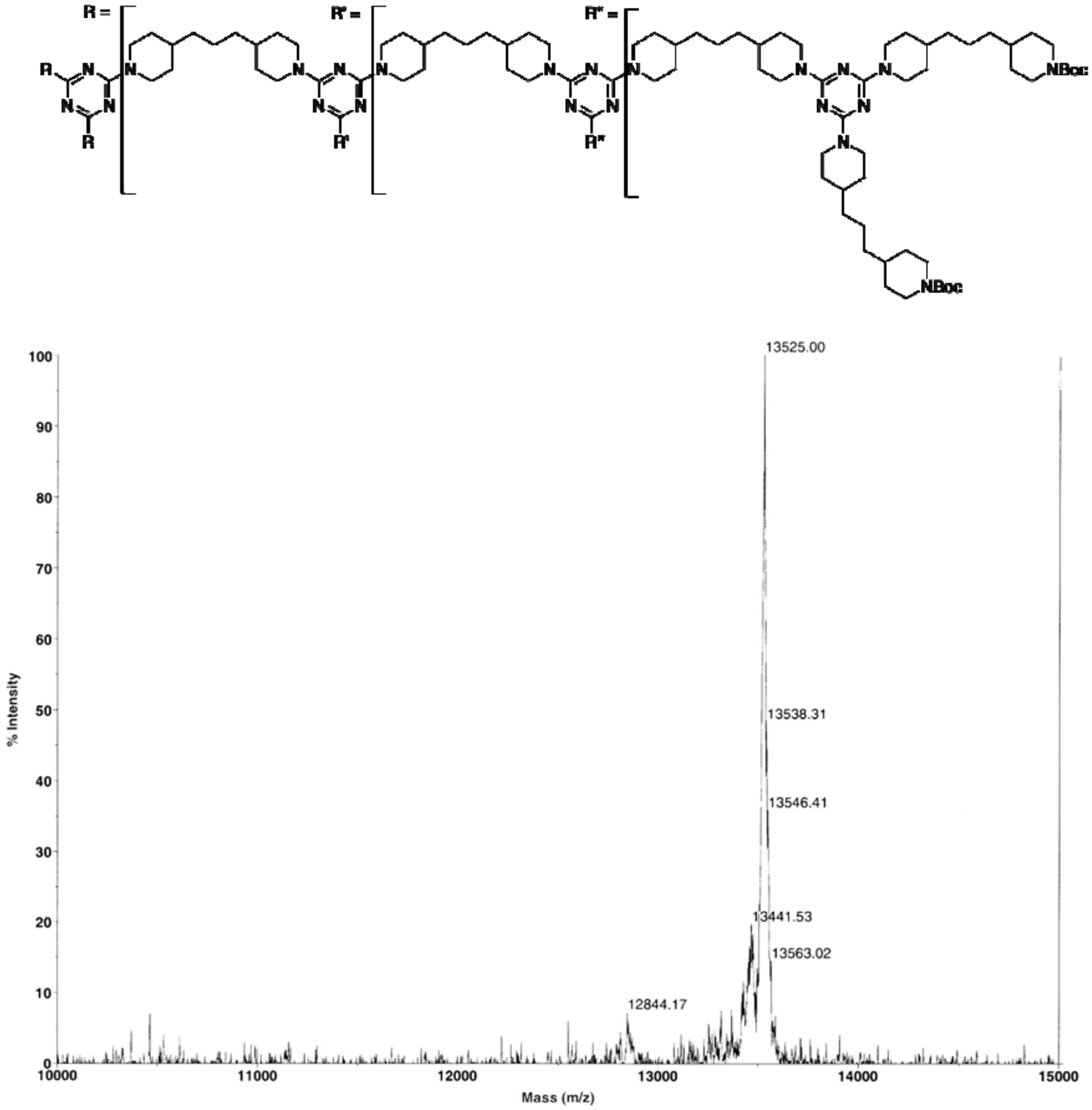
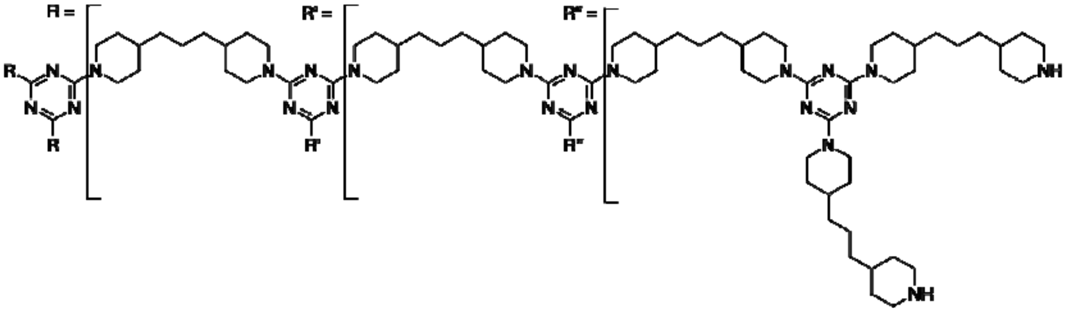


Figure S27. MALDI mass spectrum of dendrimer **9**.



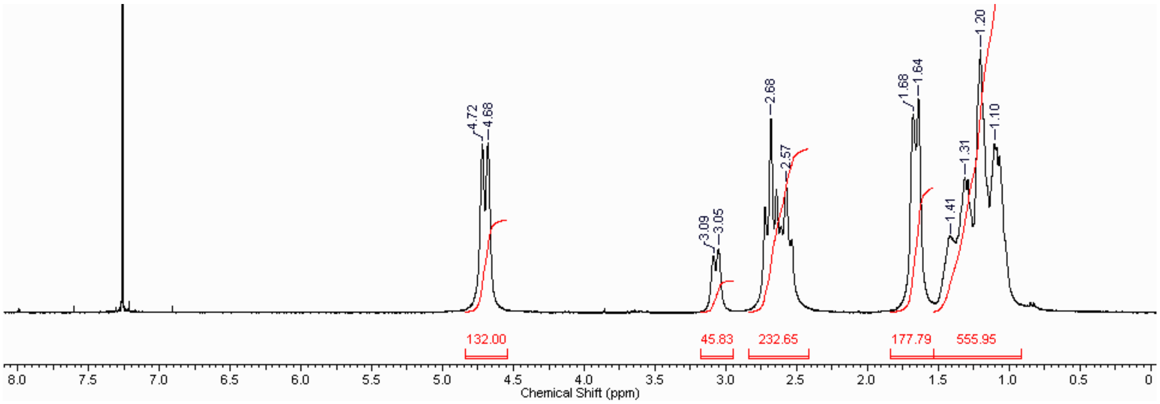


Figure S28. ^{1}H NMR spectrum of dendrimer **10** (300 MHz, CDCl$_3$).

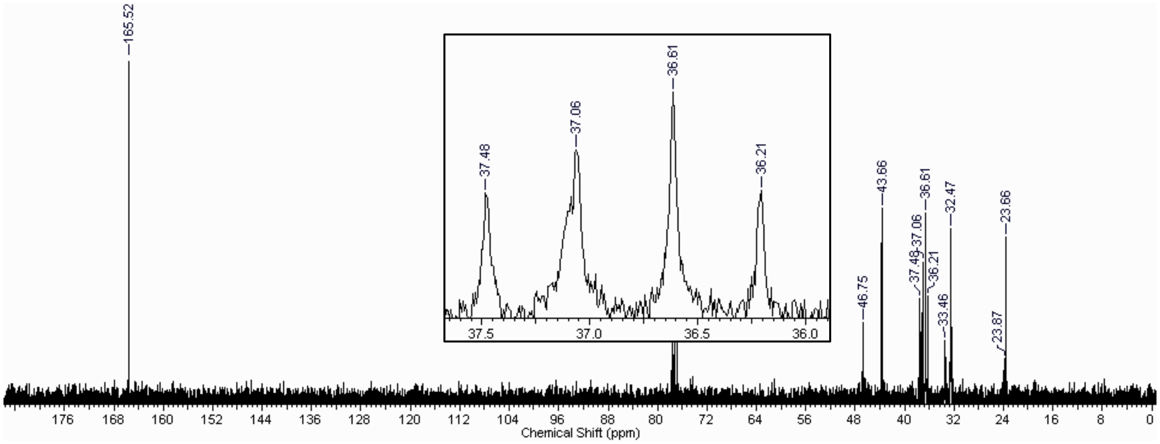
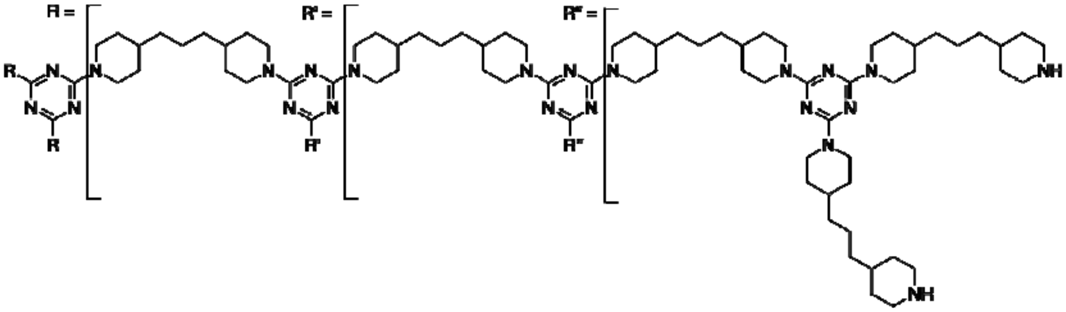


Figure S29. ^{13}C NMR spectrum of dendrimer **10** (75 MHz, CDCl$_3$).



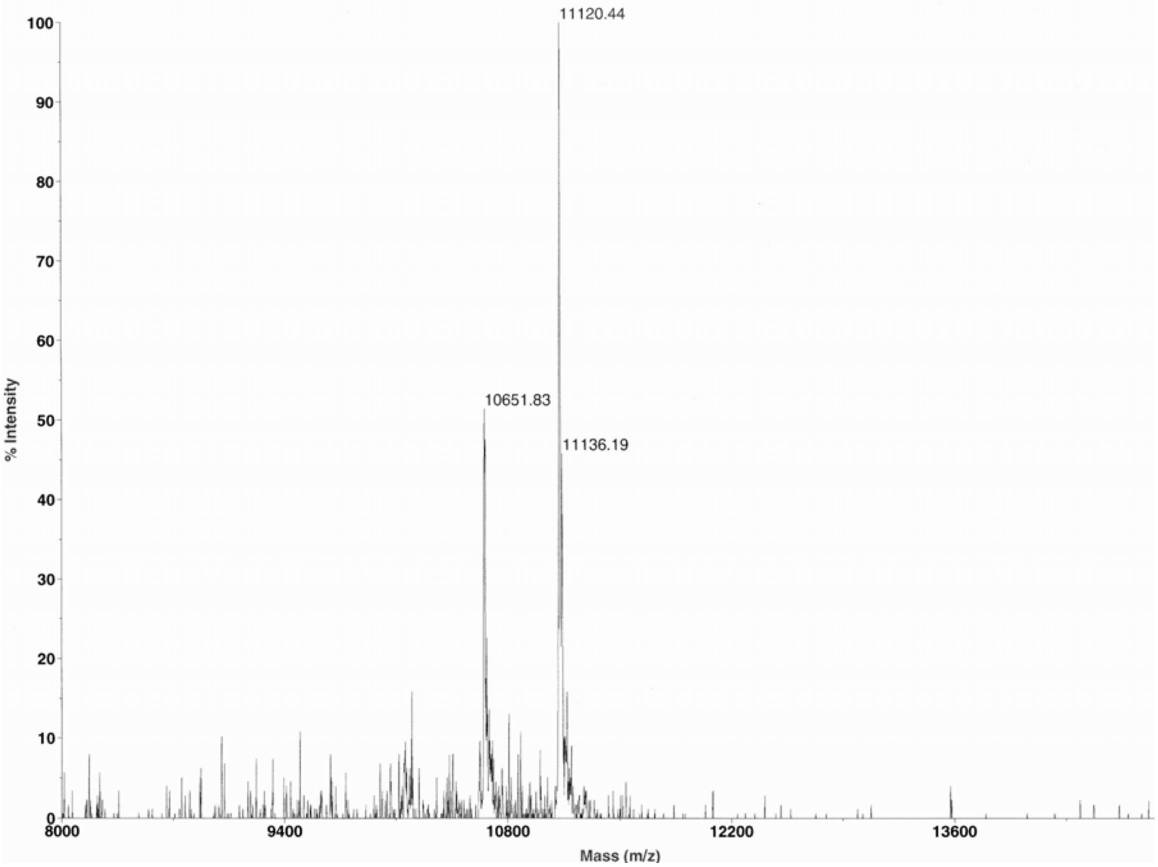


Figure S30. MALDI mass spectrum of dendrimer **10**.

Experimental Procedures

Compound S1. Boc-anhydride (2.43g, 11.15 mmol) and 4,4-trimethylene-dipiperidine (3.6 g, 17.09 mmol) were each dissolved in 150 mL CH_2Cl_2 and cooled to 0 °C. The Boc-anhydride solution was added dropwise to the diamine solution over 1 hr, followed by the addition of triethylamine (5 mL, 28 mmol). The reaction mixture was allowed to warm to room temperature. After 12 hr, the reaction was condensed and purified by column chromatography (5:1 CH_2Cl_2:CH_3OH → 5:1 CH_2Cl_2:CH_3OH with 2% NH_4OH) to afford **1** (1.55 g, 45%). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.01 (b, 2H, equatorial C**H**NBoc), 3.05 (t, 2H, equatorial C**H**NH), 2.57 (m, 4H, axial C**H**NBoc, C**H**NH), 1.60 (t, 4H, equatorial $C\mathbf{H_2}CH_2N$), 1.40 (s, 9H, $C(C\mathbf{H_3})$), 1.26 (m, 4H, $C\mathbf{H_2}CH_2C\mathbf{H_2}$), 1.16 (m, 6H, $CH_2C\mathbf{H_2}CH_2$, C**H**trimethylene), 1.02 (m, 4H, axial $C\mathbf{H}CH_2NH$, axial $C\mathbf{H}CH_2NBoc$). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 154.9 (**C**O), 79.1 ($\mathbf{C}(CH_3)_3$), 46.5 ($\mathbf{C}H_2NH$), 44.4 ($\mathbf{C}H_2NBoc$), 37.3 ($CH_2CH_2\mathbf{C}H_2$), 36.7 ($\mathbf{C}H_2CH_2CH_2$), 36.0 (**C**Htrimethylene), 33.2 ($\mathbf{C}H_2CH_2NH$), 32.2 ($\mathbf{C}H_2CH_2NBoc$), 28.5 ($C(\mathbf{C}H_3)_3$), 23.5 ($CH_2\mathbf{C}H_2CH_2$). MS (ESI): calcd 310.3 (M^+); found 311.3 ($M + H^+$).

Compound 1. Cyanuric chloride (0.27 g, 1.49 mmol) and compound **S1** (1.02 g, 3.29 mmol) were each dissolved in 25 mL CH_2Cl_2. Diisopropylethylamine (2.9 mL, 16.5 mmol) was added to the solution of **S1**. The solution of **S1** and DIPEA was added dropwise to cyanuric chloride at 0 °C, and the reaction mixture was allowed to warm to room temperature. After 12 hr, the reaction was washed with distilled water, dried, and purified by column chromatography (30:1 CH_2Cl_2:EtOAc → 10:1 CH_2Cl_2:EtOAc) to afford **1** (1.44 g, 93%). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.63 (d, 4H, equatorial C**H**N-triazine), 4.03 (b, 4H, equatorial C**H**NBoc), 2.75-2.64 (m, 8H, axial C**H**NBoc, axial C**H**N-triazine), 1.68-1.63 (d, 8H, equatorial $C\mathbf{H_2}CH_2N$), 1.43 (s, 18H, $C(C\mathbf{H_3})$), 1.29 (m, 8H, $C\mathbf{H_2}CH_2C\mathbf{H_2}$), 1.20 (m, 8H, $CH_2C\mathbf{H_2}CH_2$, C**H**trimethylene), 1.05 (m, 8H, axial $C\mathbf{H}CH_2Ntriazine$, axial $C\mathbf{H}CH_2NBoc$). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.6 ($N_3\mathbf{C}_3$), 164.2 (N_3C_3), 155.0 (**C**O), 79.3 ($\mathbf{C}(CH_3)_3$), 44.2 ($\mathbf{C}H_2NBoc$), 44.0 ($\mathbf{C}H_2N$-triazine), 36.8 ($CH_2CH_2CH_2$), 36.8 ($\mathbf{C}H_2CH_2CH_2$), 36.3-36.1 (**C**Htrimethylene), 32.3 ($\mathbf{C}H_2CH_2N$), 28.6 ($C(\mathbf{C}H_3)_3$), 23.7 ($CH_2\mathbf{C}H_2CH_2$). MS (ESI): calcd 731.5 (M^+); found 732.6 ($M + H^+$).

Compound 3. Cyanuric chloride (0.25 g, 1.37 mmol) and compound **1** (1.41 g, 4.53 mmol) with diisopropylethylamine (4.0 mL, 23 mmol) were each dissolved in 20 mL THF at room temperature and heated to reflux. After 24 hr, the reaction mixture was dried, dissolved in chloroform, and washed three times with distilled water. The organic layer was dried and purified by column chromatography (30:1 CH_2Cl_2:EtOAc → 5:1 CH_2Cl_2:EtOAc) to afford **3** (0.78 g, 57%). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.68 (d, 6H, equatorial C**H**N-triazine), 4.05 (b, 6H, equatorial C**H**NBoc), 2.68 (m, 12H, axial C**H**NBoc, axial C**H**N-triazine), 1.64 (d, 12H, equatorial $C\mathbf{H_2}CH_2N$), 1.44 (s, 27H, $C(C\mathbf{H_3})$), 1.30 (m, 12H, $C\mathbf{H_2}CH_2C\mathbf{H_2}$), 1.21 (m, 12H, $CH_2C\mathbf{H_2}CH_2$, C**H**trimethylene,), 1.06 (m, 12H, axial $C\mathbf{H}CH_2Ntriazine$, axial $C\mathbf{H}CH_2NBoc$). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 165.4 ($N_3\mathbf{C}_3$), 155.0 (**C**O), 79.2 ($\mathbf{C}(CH_3)_3$), 44.3 ($\mathbf{C}H_2NBoc$), 43.5 ($\mathbf{C}H_2N$-triazine), 36.9 ($CH_2CH_2\mathbf{C}H_2$), 36.7 ($\mathbf{C}H_2CH_2CH_2$), 36.4-36.0 (**C**Htrimethylene), 32.3 ($\mathbf{C}H_2CH_2N$), 28.5 ($C(\mathbf{C}H_3)_3$), 23.6 ($CH_2\mathbf{C}H_2CH_2$). MS (MALDI): calcd 1005.8 (M^+); found 1007.1 ($M + H^+$).

Compound 4. Compound **3** (0.52 g, 0.52 mmol) was dissolved in 10 mL CH_3OH. Concentrated HCl (10 mL) was added to the reaction mixture. After 18 hr, the reaction mixture was dried, basified with 5 M NaOH, and extracted into chloroform. The organic layer was dried to afford **4** (0.39 g, quantitative). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.67 (d, 6H, equatorial C**H**N-triazine), 3.02 (d, 6H, equatorial C**H**NH), 2.67 (t, 6H, axial C**H**Ntriazine), 2.54 (t, 6H, axial C**H**NH), 1.60 (t, 12H, equatorial $C\mathbf{H_2}CH_2N$), 1.29 (m, 12H, $C\mathbf{H_2}CH_2C\mathbf{H_2}$), 1.19 (m, 12H, $CH_2C\mathbf{H_2}CH_2$, C**H**trimethylene), 1.02 (m, 12H, axial $C\mathbf{H}CH_2N$). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 165.5 ($\mathbf{C}_3N_3$), 47.0 ($\mathbf{C}H_2NH$), 43.6 ($\mathbf{C}H_2N$-triazine), 37.6 ($CH_2CH_2\mathbf{C}H_2$), 37.0 ($\mathbf{C}H_2CH_2CH_2$), 36.6-36.4 (**C**Htrimethylene), 33.9 ($\mathbf{C}H_2CH_2NH$), 32.5 ($\mathbf{C}H_2CH_2N$-triazine), 23.7 ($CH_2\mathbf{C}H_2CH_2$). MS (ESI): calcd 705.6 (M^+); found 706.8 ($M + H^+$).

Compound 5. Monochlorotriazine **1** (0.37 g, 0.50 mmol) and compound **4** (0.11 g, 0.15 mmol) were each dissolved in 5 mL THF. Diisopropylethylamine (0.9 mL, 5 mmol) was added to the solution of **4**. The monochlorotriazine solution was added to the solution of **4**, and the reaction mixture was heated to reflux. After 24 hr, the reaction mixture was dried, dissolved in chloroform, and washed three times with distilled water. The organic layer was dried, and the solid was purified by column chromatography (30:1 CH_2Cl_2:EtOAc → 5:1 CH_2Cl_2:EtOAc) to afford **5** (0.25 g, 80% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.68 (d, 24H, equatorial C**H**N-triazine), 4.05 (b, 12H, equatorial C**H**NBoc), 2.68 (m, 36H, axial C**H**NBoc, axial C**H**N-triazine), 1.64 (d, 36H, equatorial $C\mathbf{H_2}CH_2N$), 1.44 (s, 54H, $C(C\mathbf{H_3})$), 1.32 (m, 36H, $C\mathbf{H_2}CH_2C\mathbf{H_2}$), 1.21 (m, 36H, $CH_2C\mathbf{H_2}CH_2$, C**H**trimethylene,), 1.06 (m, 36H, axial $C\mathbf{H}CH_2N$triazine, axial $C\mathbf{H}CH_2NBoc$). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 165.5 ($N_3\mathbf{C}_3$), 155.1 (**CO**), 79.3 ($\mathbf{C}(CH_3)_3$), 44.1 ($\mathbf{C}H_2NBoc$), 43.6 ($\mathbf{C}H_2N$-triazine), 37.0 ($CH_2CH_2\mathbf{C}H_2$), 36.9 ($\mathbf{C}H_2CH_2CH_2$), 36.6-36.1 (**C**Htrimethylene), 32.5 ($\mathbf{C}H_2CH_2N$), 28.7 ($C(\mathbf{C}H_3)_3$), 23.8 ($CH_2\mathbf{C}H_2CH_2$). MS (MALDI): calcd 2792.1 (M^+); found 2792.0 ($M + H^+$).

Compound 6. Compound **5** (0.20 g, 0.07 mmol) was dissolved in 5 mL CH_3OH. Concentrated HCl (5 mL) was added, and the reaction mixture was stirred at room temperature. After 12 hr, the reaction mixture was dried and precipitated with 5 M NaOH. The precipitate was filtered and dried to afford **6** (0.16 g, quantitative). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.67 (d, 24H, equatorial C**H**N-triazine), 3.03 (d, 12H, equatorial C**H**NH), 2.67 (t, 24H, axial C**H**Ntriazine), 2.54 (t, 12H, axial C**H**NH), 1.64 (m, 36H, equatorial $C\mathbf{H_2}CH_2N$), 1.29 (m, 36H, $C\mathbf{H_2}CH_2C\mathbf{H_2}$), 1.19 (m, 36H, $CH_2C\mathbf{H_2}CH_2$, C**H**trimethylene), 1.02 (m, 36H, axial $C\mathbf{H}CH_2N$). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 165.5 ($\mathbf{C}_3N_3$), 47.0 ($\mathbf{C}H_2NH$), 43.6 ($\mathbf{C}H_2N$-triazine), 37.6 ($CH_2CH_2\mathbf{C}H_2$), 37.1 ($\mathbf{C}H_2CH_2CH_2$), 36.6-36.4 (**C**Htrimethylene), 33.8 ($\mathbf{C}H_2CH_2NH$), 32.5 ($\mathbf{C}H_2CH_2N$-triazine), 23.6 ($CH_2\mathbf{C}H_2CH_2$). MS (MALDI): calcd 2191.8 (M^+); found 2191.6 ($M + H^+$).

Compound 7. Monochlorotriazine **1** (0.60 g, 0.81 mmol) and dendrimer **6** (0.19 g, 0.09 mmol) were each dissolved in 1.5 mL THF. Diisopropylethylamine (1.4 mL, 8.0 mmol) was added to the solution of **6**. The monochlorotriazine solution was added to the solution of **6**, and the reaction mixture was heated to reflux. After 48 hr, the reaction mixture was dried, dissolved in chloroform, and washed three times with distilled water. The organic layer was dried, and the solid was purified by column chromatography (30:1

CH_2Cl_2:EtOAc → 5:1 CH_2Cl_2:EtOAc) to afford **7** (0.37 g, 73% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.69 (d, 60H, equatorial C**H**N-triazine), 3.06 (b, 24H, equatorial C**H**NBoc), 2.69 (m, 84H, axial C**H**NBoc, axial C**H**N-triazine), 1.65 (m, 84H, equatorial C**H$_2$**CH_2N), 1.44 (s, 108H, C(C**H$_3$**)), 1.32 (m, 84H, C**H$_2$**CH_2C**H$_2$**), 1.21 (m, 84H, CH_2C**H$_2$**CH_2, C**H**trimethylene,), 1.06 (m, 84H, axial C**H**CH_2Ntriazine, axial C**H**CH_2NBoc). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 165.5 (N_3**C$_3$**), 155.1 (**C**O), 79.3 (**C**(CH_3)$_3$), 44.3 (**C**H_2NBoc), 43.7 (**C**H_2N-triazine), 37.1 (CH_2CH_2**C**H_2), 36.9 (**C**$H_2CH_2CH_2$), 36.6-36.1 (**C**Htrimethylene), 32.5 (**C**H_2CH_2N), 28.7 (C(**C**H_3)$_3$), 23.8 (CH_2**C**H_2CH_2). MS (MALDI): calcd 6364.9 (M^+); found 6376.0 ($M + H^+$).

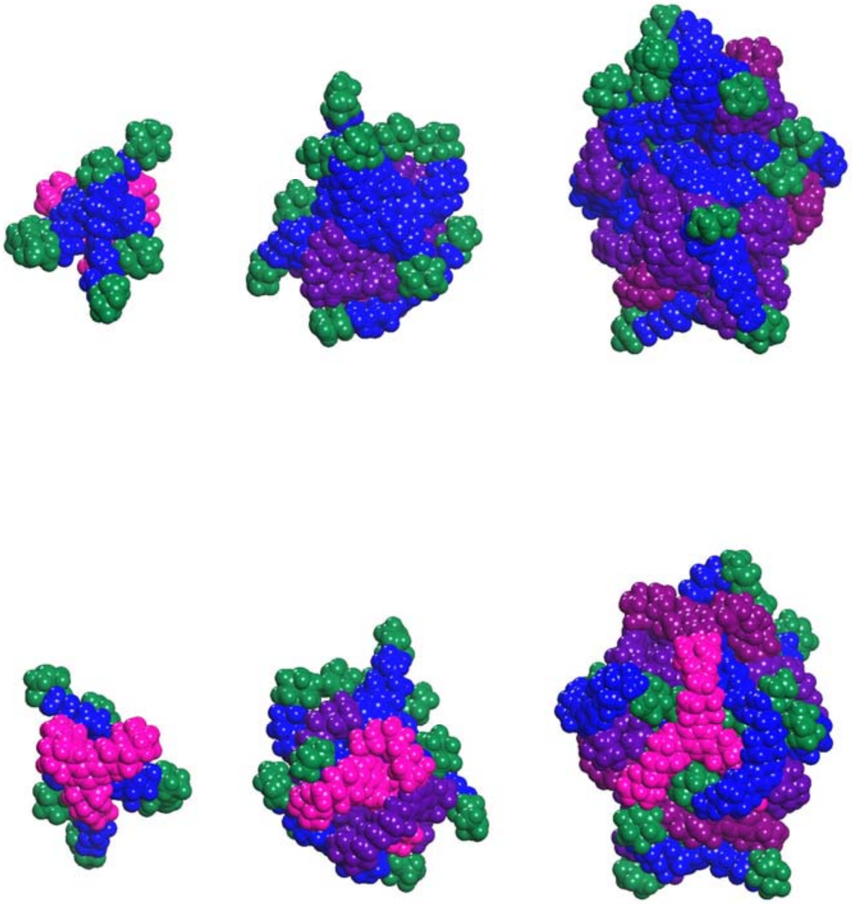
Compound 8. Dendrimer **7** (0.37 g, 0.06 mmol) was dissolved in 5 mL CH_3OH. Concentrated HCl (5 mL) was added, and the reaction mixture was stirred at room temperature. After 10 hr, the reaction mixture was dried and precipitated with 5 M NaOH. The precipitate was filtered and dried to afford **8** (0.29 g, 98%). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.70 (d, 60H, equatorial C**H**N-triazine), 3.12 (d, 24H, equatorial C**H**NH), 2.68 (t, 60H, axial C**H**Ntriazine), 2.60 (t, 24H, axial C**H**NH), 1.67 (m, 84H, equatorial C**H$_2$**CH_2N), 1.31 (m, 84H, C**H$_2$**CH_2C**H$_2$**), 1.21 (m, 84H, CH_2C**H$_2$**CH_2, C**H**trimethylene), 1.10 (m, 84H, axial C**H**CH_2N). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 165.5 (**C$_3$**N_3), 46.5 (**C**H_2NH), 43.7 (**C**H_2N-triazine), 37.4 (CH_2CH_2**C**H_2), 37.0 (**C**$H_2CH_2CH_2$), 36.6-36.0 (**C**Htrimethylene), 33.1 (**C**H_2CH_2NH), 32.5 (**C**H_2CH_2N-triazine), 23.6 (CH_2**C**H_2CH_2). MS (MALDI): calcd 5164.3 (M^+); found 5165.7 ($M + H^+$).

Compound 9. Monochlorotriazine **1** (0.22 g, 0.30 mmol) and dendrimer **8** (0.10 g, 0.02 mmol) were each dissolved in 1.5 mL THF. Diisopropylethylamine (0.5 mL, 3 mmol) was added to the solution of **S1**. The monochlorotriazine solution was added to the solution of **8**, and the reaction mixture was heated to reflux. After 48 hr, the reaction mixture was dried, dissolved in chloroform, and washed three times with distilled water. The organic layer was dried, and the solid was purified by column chromatography (10:1 CH_2Cl_2:EtOAc → 1:1 CH_2Cl_2:EtOAc) to afford **9** (0.16 g, 70% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.68 (d, 132H, equatorial C**H**N-triazine), 4.05 (b, 48H, equatorial C**H**NBoc), 2.68 (m, 180H, axial C**H**NBoc, axial C**H**N-triazine), 1.64 (m, 180H, equatorial C**H$_2$**CH_2N), 1.44 (s, 216H, C(C**H$_3$**)), 1.30 (m, 180H, C**H$_2$**CH_2C**H$_2$**), 1.21 (m, 180H, CH_2C**H$_2$**CH_2, C**H**trimethylene,), 1.06 (m, 180H, axial C**H**CH_2Ntriazine, axial C**H**CH_2NBoc). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 165.5 (N_3**C$_3$**), 155.1 (**C**O), 79.3 (**C**(CH_3)$_3$), 44.0 (**C**H_2NBoc), 43.6 (**C**H_2N-triazine), 37.0 (CH_2CH_2**C**H_2), 36.9 (**C**$H_2CH_2CH_2$), 36.6-36.1 (**C**Htrimethylene), 32.5 (**C**H_2CH_2N), 28.7 (C(**C**H_3)$_3$), 23.8 (CH_2**C**H_2CH_2). MS (MALDI): calcd 13510.4 (M^+); found 13505.4 ($M + H^+$).

Compound 10. Dendrimer **9** (0.06 g, 4.3 μmol) was dissolved in 2.5 mL CH_3OH. Concentrated HCl (2.5 mL) was added, and the reaction mixture was stirred at room temperature. After 16 hr, the reaction mixture was dried and precipitated with 5 M NaOH. The precipitate was filtered and dried to afford **10** (0.04 g, 75%). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.70 (d, 132H, equatorial C**H**N-triazine), 3.07 (d, 48H, equatorial C**H**NH), 2.68 (t, 132H, axial C**H**Ntriazine), 2.60 (t, 48H, axial C**H**NH), 1.66 (d, 180H, equatorial C**H$_2$**CH_2N), 1.31 (m, 180H, C**H$_2$**CH_2C**H$_2$**), 1.21 (m, 180H, CH_2C**H$_2$**CH_2, C**H**trimethylene), 1.10 (m, 180H, axial C**H**CH_2N). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 165.5

($\mathbf{C}_3N_3$), 46.5 ($\mathbf{C}H_2NH$), 43.7 ($\mathbf{C}H_2N$-triazine), 37.4 ($CH_2CH_2\mathbf{C}H_2$), 37.0 ($\mathbf{C}H_2CH_2CH_2$), 36.6-36.0 ($\mathbf{C}$Htrimethylene), 33.1 ($\mathbf{C}H_2CH_2NH$), 32.5 ($\mathbf{C}H_2CH_2N$-triazine), 23.6 ($CH_2\mathbf{C}H_2CH_2$). MS (MALDI): calcd 11109.1 (M^+); found 11120.4 ($M + H^+$).

Gas Phase Computational Models of Deprotected Dendrimers



Protected dendrimers (not shown here):

3 Rg = 8.56 Angstroms (Diameter = 17.12 Angstroms)
5 Rg = 11.12 Angstroms (Diameter = 22.24 Angstroms)
7 Rg = 14.13 Angstroms (Diameter = 28.23 Angstroms)

Derotected dendrimers: pink - core, green – surface piperdine, peripheral layer (blue); interior layer (raspberry) (shown here)

4 = 8.83 Angstroms (Diameter = 17.66 Angstroms)
6 Rg = 10.51 Angstroms (Diameter = 21.02 Angstroms)
8 Rg = 13.60 Angstroms (Diameter = 27.20 Angstroms)